ORIGINAL ARTICLE

Thoracoamniotic shunting for fetal pleural effusions using a double-basket shunt

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ABSTRACT

Objective To describe the safety and efficacy of thoracoamniotic shunting for fetal pleural effusion using a double-basket catheter with a very small diameter (1.47 mm).

Method In this 2-year multicenter, prospective single-arm clinical study registered with the University hospital Medical Information Network (UMIN) Clinical Trials Registry (UMIN00001095); shunting was performed between 18w0d and 33w6d of gestation with this catheter in cases of fetal pleural effusions reaccumulating after thoracocentesis. The primary endpoint measures were maternal and fetal adverse effects and survival in the neonatal period.

Results A total of 24 cases were included, of which 17 had hydrops (71%). The median gestational ages at shunting and delivery were 27.4 and 34.8 weeks, respectively. There were no fetal deaths, lung injuries, or severe maternal complications. Preterm rupture of the membranes occurred in 7/24 (29%) cases at a median of 62 days after the shunting. Preterm rupture of the membranes within 28 days of the procedure occurred in 1/24 (4%) cases. Catheter displacement towards the fetal thoracic cavity occurred in 4/42 (10%) cases. The overall survival rate was 79% (19/24), whereas it was 71% (12/17) in the cases with hydrops.

Conclusion Drainage of fetal pleural effusions with a double-basket shunt is safe and effective, and the shunt could be an alternative device. © 2012 John Wiley & Sons, Ltd.

Funding sources: This work was supported by a grant from The Ministry of Health, Labour and Welfare of Japan (Health and Labour Sciences Research Grants of Clinical Research for New Medicine).
Conflicts of interest: None declared

INTRODUCTION

The prognosis of untreated isolated fetal pleural effusion associated with hydrops is still poor[1–3]; the estimated survival rate of such cases is only around 22–53%.[3] Fetal interventions in cases of recurrent pleural effusion, such as single or serial thoracocentesis, primary thoracoamniotic shunting (TAS), or TAS after initial thoracocentesis, have also been shown to yield similar outcomes.[4] In one review, spontaneous recovery was reported in 22% of cases.[2] Reaccumulation of pleural effusion after thoracocentesis might be considered as a more pragmatic indication for fetal intervention. In 1990, a 'double-basket shunt ' (Hakko Co., Nagano, Japan, Figure 1) was developed in Japan and because it has been frequently used for TAS in that country. There are only sporadic case reports on this device, whereas larger series are lacking.[5–7] Herein, we report on a prospective multicenter study on TAS for fetal pleural effusion using this double-basket shunt.

MATERIALS AND METHODS

Study design

This was a 2-year prospective multicenter single-arm clinical study registered with University hospital Medical Information Network (UMIN) Clinical Trials Registry (UMIN00001095), which is a study conducted with the aim of determining the safety and efficacy of TAS using the double-basket catheter. Five fetal medicine units in Japan participated: the National Center for Child Health and Development (Tokyo), Nagara Medical Center (Gifu), Yamaguchi University Hospital

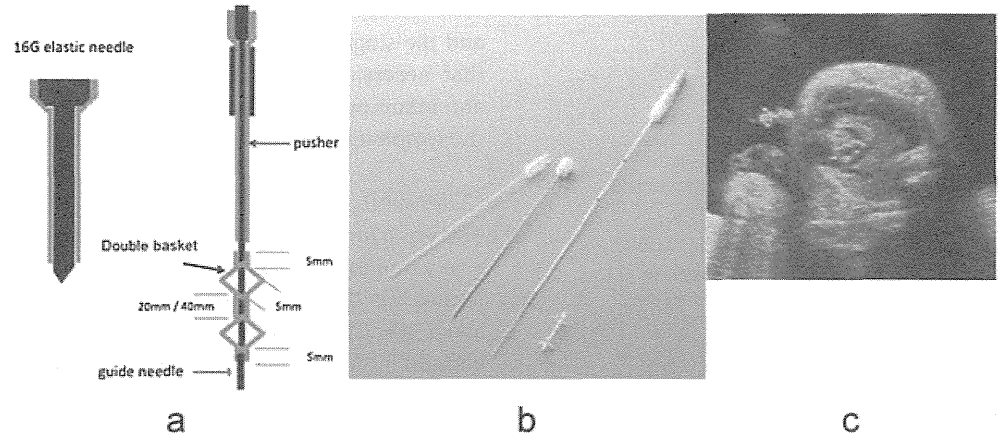

Figure 1 The double-basket catheter. (a) Schema of the double-basket catheter developed by Hakko, Japan; (b) A picture of the trocar and the inner cannula; (c) An ultrasonographic image obtained just after the shunting operation

(Ube), Seirei Hamamatsu General Hospital (Hmamatsu), and the National Cerebral Cardiovascular Center (Osaka). Data were gathered by an independent data-coordinating center at the Japan Clinical Research Support Unit. The study was conducted with the approval of the institutional review board at each center. All patients provided written informed consent.

Pregnant women aged 16–45 years old with a singleton pregnancy between 18w0d and 33w6d were asked to participate. Further inclusion criteria were fetal unilateral or bilateral pleural effusion (effusion area occupying more than half of the fetal chest area) of the fetus that was either isolated (fetal chylothorax) or associated with pulmonary sequestration[7] and showed reaccumulation to the previous level within 7 days after the initial thoracocentesis. The exclusion criteria were major fetal anomalies that could independently affect the chances of neonatal survival. Fetal karyotyping was offered, but was not essential for study entry. Minor fetal anomalies, for example, cleft lip, ventricular septal defect, or polydactyly, were not counted as exclusion criteria. The other exclusion criteria were hydrops because of other causes such as fetal arrhythmias, viral infections (cytomegalovirus, parvovirusB19), and blood-type incompatibility, women with severe maternal complications, such as pregnancy-induced hypertension, mirror syndrome[8–10] associated with hydrops fetalis, or placental thickness >6 cm, cases with a shortened cervix (<10 mm), genital bleeding, or preterm rupture of the membranes (PROM) before the procedure, and cases with a previous history of amniocentesis or amnioreduction. Hydrops fetalis was defined as the presence of skin edema at the head (>5 mm) or accumulation of fluid other cavities (such as ascites or pericardial effusion) in addition to the pleural effusion.

Interventions

We performed TAS within 7 days after the initial thoracocentesis. If the effusion was bilateral, we attempted to insert the TAS catheter on both sides, unless there were obvious technical restrictions. The number of attempts was empirically set at a maximum of three times for each side. The procedure was conducted after administration of a tocolytic drug (ritodorine chloride 50 μg/min i.v.), and the preferred anesthetic technique was local anesthesia. If necessary, a maternal sedative (diazepam i.v. or pentazocine hydrochloride i.m.) was given. In the presence of excessive fetal movements, maternal general anesthesia ($n=2$) or fetal muscular injection of vecuronium bromide ($n=4$) was used. A 16G puncture cannula with a sharp trocar (inner/outer diameter 1.66/2.14 mm; EV16GX 250 mm/150 mm, Hakko Co., Nagano, Japan) was inserted through the maternal abdominal and uterine wall and through the fetal chest wall into the effusion under ultrasound guidance. The preferential insertion site was the lateral chest wall, and the tip of the needle was kept about 10 mm from the fetal chest wall. After confirming flow of the fluid via the cannula, the double-basket catheter was advanced with a pusher through the trocar about 15 mm beyond the tip, until opening of the distal basket could be confirmed by ultrasound. Thereafter, the cannula was withdrawn over the pusher so that the proximal basket would open (shunt tube inner diameter 0.9 mm, outer diameter 1.47 mm; Hakko Co.). Finally, the pusher and cannula were removed (Figure 1). A prophylactic antibiotic (cefazolin 1 g i.v. at the time of the procedure) was also administered.

Follow-up ultrasound and Doppler examination was performed at 1, 3, and 7 days and weekly thereafter until delivery. Standard antenatal corticosteroid therapy (betamethasone 12 mg i.m. twice with a 24-h interval between the two injections) was provided for preterm delivery before 34 weeks of gestation,[11] with the delivery timing decided on the basis of obstetrical indications.

Endpoints and sample size

The primary endpoint measures were maternal and fetal adverse effects (AEs) and the survival rate in the neonatal period (28 days of life). In the cases with hydrops, improvement of the fetal skin edema at the final assessment just before delivery {classified as either (1) complete remission (disappearance of the edema), (2) partial remission [edema decreased, but still persisting to some degree, (3) no change, or (4) progression]}, and other perinatal outcomes. The anticipated survival rate was assumed to be 70% empirically, and with a sample size of 20 patients, and the lower 90% confidence limit would be above 50%.[12]

RESULTS

A total of 24 women were enrolled between April 2008 and March 2010 (24 months). The characteristics of the 24 cases are summarized in Figure 2, and details of the individual cases are

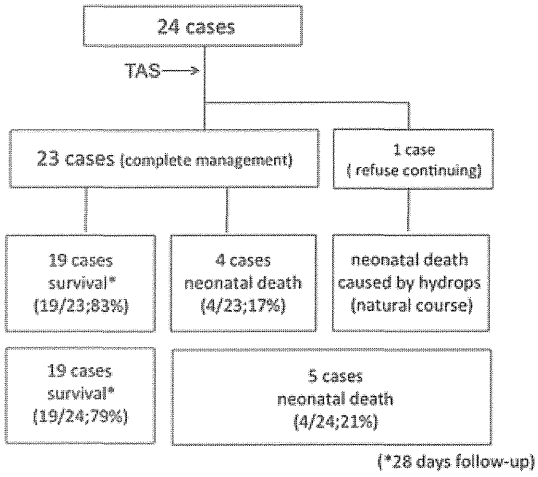

Figure 2 Chart of prospective registered study. TAS, thoracoamniotic shunting

presented in Table 1. The median gestational age at TAS was 27.4 weeks (interquartile range 26.2–31.2). Hydrops was observed in 71% of the cases. Umbilical arterial Doppler revealed abnormalities in 2/24 cases (8%), and none had abnormal ductus venosus. Ten had bilateral pleural effusions (Table 2), and a bilateral shunt was placed in six of these cases. In the remaining four cases of bilateral and 14 cases of unilateral effusion, a shunt could be placed successfully. There were 42 candidate cavities, and the procedure was finally successfully performed in 39 (93%). In one patient, chromosome 6 monosomy was detected after the first shunt, not associated with any visible morphological abnormalities. The family did not desire a second shunt operation (Table 1), as the first did not improve the fetal condition completely, and the patient discontinued the management.

The overall survival rate at 28 days of life was 79% (90% confidence interval, 61.1–91.4%). The median gestational age at delivery was 34.8 weeks (interquartile range). For the fetuses with hydrops, the neonatal survival rate was 71% (90% confidence interval, 47.8–87.6%; $n=12$). Complete remission occurred in 7/16 (42.8%) cases, and partial remission in 4/16 (25%) cases (Table 3).

The catheter-related outcomes and complications are shown in Table 4. There were 34 candidate cavities (unilateral 14, bilateral 10×2) and a total of 42 sessions, including reinterventions. When we analyzed the time-lag for the reintervention (at least 2 days after first shunt), the rate per patient was 8/24 (33%). Catheter displacement into the thoracic cavity occurred in 4/42 sessions. In all of these cases, it was successfully removed by surgery after birth. The two catheters that did not function in utero were found after birth to have fibrin obstruction. The PROM rate within 28 days after the TAS was 4.2% (1/24). There were no cases of intrauterine infection or abruptio placentae. There were three cases of Mirror's syndrome, presenting after shunting at 28, 31, and 30 weeks gestation (Cases 4, 8, and 21 in Table 1), that necessitated immediate delivery and maternal intensive care for lung edema ($n=3$), and maternal pleural effusion ($n=3$); however, all recovered without sequelae. However, neonatal death occurred in two of the three cases of Mirror's syndrome, and the single surviving case showed severe pleural effusion that necessitated prolonged intensive care in the neonatal and infant period, after the diagnosis of congenital aplasia of the lymphatic vessels was made (Case 8).

COMMENT

This was a prospective trial of TAS for fetal pleural effusion using a very thin double-basket shunt. The overall survival rate of the fetuses was 79%, and the survival rate in those with hydrops was about 71%. The reported survival rate of the fetuses with pleural effusion in the absence of fetal intervention is 59%, and that in the fetuses with hydrops is 35%.[13–15] Fetal therapy using the double-basket shunt for pleural effusions seems to be as effective as that reported for other shunts.

The most striking observation of the present study was that there were no fetal deaths. Reported fetal death rates from other series are 20/125 (16%),[13] 8/21(38%),[14] and 9/54 (16%);[15] however, no detailed case profiles have been reported that could allow a reasonable discussion. One retrospective report indicated a PROM rate of 15% (7/27).[15] In our series, the PROM rate was 1/24 within 28 days (4.2%) of the TAS, and the overall PROM rate was 7/24 (29%). Interestingly, the median gestational week at delivery was 34 weeks in both our study and the aforementioned review.[3]

The risk associated with a catheter has been reported to be correlated with the size of the catheter.[3,13,16] The trocar for inserting the double-basket shunt has an inner diameter of 1.66 mm and outer diameter 2.14 mm (16G). The shunting catheter itself has an inner diameter of 0.9 mm and outer diameter of 1.47 mm, which is the thinnest available for fetal shunting at the moment present. However, the reintervention rate in our study was high (23% per procedures and 33% time-lag reintervention per cases). Shunt failure can be caused by obstruction or displacement, potentially caused by the softness of the catheter. However, in four of the five neonatal death cases, we performed once for each cavity (Table 1). Therefore, the reintervention itself did not seem to be related with a poor neonatal prognosis. There were four cases of catheter displacement into the fetal chest cavity, and the catheter could be removed surgically without any adverse outcomes in all cases. In summary, use of this thin polyethylene shunt could be associated with a higher rate of failure, even though the catheter seemed atraumatic. The most widely used catheter is the silicone double pigtail catheter (Rocket of London Ltd, Watford, UK; inner diameter 2.1 mm, outer diameter 3.0 mm).[16–18] Other devices, such as the Harrison shunt (Cook Urological, Spencer, Ind., USA; inner and outer diameter 0.97 mm and 1.67 mm) and the 4F-angiographic single pigtail catheter (Cordis, Johnson & Johnson, The Netherlands) have been also used.[19] When the outcomes were compared, there were no significant differences in the survival rates (around 62–66% 14 vs. 70% in the hydropic fetuses in our series). The reintervention rate in our series was 23–33% and in those reported series were specifically mentioned 3/9 (33%) and 8% (4/49), respectively.[20,21] The reported rate of intrathoracic displacement is 20% (3/15)[19] as compared with the rate of 10% (4/42) in our series.

Complete remission of skin edema occurred in 7/16 fetuses (44%) and partial remission in 4/16 (25%) fetuses. Remission

Table 1 **Profiles of all registered cases of thoracoamniotic shunting**

NO	GA registration (week)	Indication	Total trials (N)	Final success (N)	Time-lag trials (times)	Preope edema	Preope ascites	Postope pl. effusion	Postope edema	Postope ascites	GA delivery (week)	Prognosis 28 days	Note
1	30	L	1	1	0	+	+	CR	CR	CR	40	Alive	
2	28	bil	2	2	1	–	–	NC	–	–	35	Alive	
3	32	bil	2	2	0	+	–	NC	Progress	–	35	Died	Severe PPHN
4	26	L	1	1	0	+	+	CR	PR	NC	28	Died	Mirror, respiratory failure
5	20	L	1	1	0	+	+	CR	CR	CR	37	Alive	
6	32	R	1	1	0	+	+	PR	PR	CR	35	Alive	
7	27	L	2	2	0	–	–	CR	–	–	34	Alive	
8	27	L	2	2	1	+	–	CR	NC	–	30	Alive	Mirror, aplasia of lymphatic vessels
9	23	R	1	1	0	+	–	Progress	Progress	Progress	36	Died	Refused therapy, 6 monosomy
10	27	bil	3	2	1	+	+	PR	CR	CR	38	Alive	
11	26	R	1	1	0	+	+	CR	CR	CR	37	Alive	
12	26	bil	4	4	2	–	+	PR	–	PR	33	Died	Severe PPHN
13	26	L	2	2	1	–	–	CR	–	–	38	Alive	
14	29	L	1	1	0	–	–	PR	–	–	31	Alive	
15	31	bil	2	2	0	+	+	PR	CR	CR	34	Alive	
16	31	bil	2	2	1	+	–	PR	PR	–	33	Alive	
17	21	L	3	3	2	+	+	Progress	CR	NC	31	Alive	
18	29	bil	1	1	0	+	+	PR	CR	CR	33	Alive	
19	32	bil	2	2	0	+	+	PR	PR	CR	34	Alive	
20	26	R	1	1	0	–	–	CR	–	–	39	Alive	
21	28	bil	1	1	0	+	–	Progress	Progress	Progress	31	Died	PROM, mirror, severe hydrops
22	25	L	4	2	2	–	–	–	–	–	28	Alive	
23	32	bil	1	1	0	+	+	Progress	NC	PR	34	Alive	
24	22	L	1	1	0	–	–	PR	–	–	36	Alive	

final success; final number of trials of succeeded thoracoamniotic shunting; NC, no change; CR, complete remission; PR, partial remission; L, left; R, right; bil, bilateral; PPHN, persistent pulmonary hypertension of neonate; PROM, preterm rupture of the membrane.

Table 2 **Baseline characteristics ($n=24$)**

Age (year)	
Median	34.5
Interquartile range	29.3–36.8
Gestational age at the first operation (week)	
Median	27.4
Interquartile range	26.2–31.2
Hydrops	17 (70.8%)
Polyhydramnios	13 (54.2%)
Side of pleural effusion	
Right	4 (16.7%)
Left	10 (41.7%)
Bilateral	10 (41.7%)
Location of placenta	
Anterior	12 (50%)
Posterior	12 (50%)

Table 3 **Perinatal outcomes ($n=24$)**

Survival rate at 28 days of life		
Hydrops	12/17 (70.6%)	
Without hydrops	7/7 (100%)	
Total	19/24 (79.2%)	
Gestational age at delivery (week)		
Median	34.8	
Interquartile range	(32–36.9)	
Birth weight (g); mean (SD)	2272 (553.7)	
Changes of skin edema after TAS		neonatal death (n)
Complete remission	7 (43.8%)	0
Partial remission	4 (25%)	1
No change	2 (12.5%)	0
Progression	3 (18.8%)	3*

SD, standard deviation; TAS, thoracoamniotic shunting.
*Included the refused case.

Table 4 **Catheter-related characteristics and complications ($n=24$)**

Number of procedures	
Total indicated cavity/trials	34/42 (1.23)
Total success rate per cavity	39/42 (93%)
Number of time-lag reintervention	8/24 (33%)
Catheter displacement	
Per case	4/24 (16.7%)
Per procedures	4/42 (9.5%)
Pregnancy complications	
Polyhydramnios after operation*	6/11 (55%)
Intrauterine infection	0 (0%)
Pregnancy-induced hypertension	1 (4.2%)
Abruption of placenta	0 (0%)
Mirror syndrome	3 (12.5%)
PROM	
Within 7 days after TAS	0 (0%)
Within 28 days after TAS	1 (4.2%)
PROM date after operation ($N=7$)	
Median (interquartile range)	62 (33–96)

PROM, preterm rupture of the membranes; TAS, thoracoamniotic shunting.
*Diagnosed polyhydramnios (Deepest vertical pool; DVP > 8 cm) after operation.

might be dependent on the interval between the fluid accumulation and the fluid drainage by the catheter. In severe cases where the catheter did not function adequately, there may have been other causes of fetal pleural effusion that are difficult to control by shunting alone. The rate of polyhydramnios after the operation seemed to be high that we confirmed additional polyhydramnios 6/11(55%) after the shunting. As we encountered cases in which polyhydramnios developed after resolution of the skin edema and effective drainage of the pleural effusion, we do not have any clear explanation for this phenomenon at present.

The survival rates and safety exceeded the acceptable level, as compared with previous reports. A double-basket shunt could be a useful alternative device for thoracoamniotic shunting in the treatment of fetal pleural effusions.

ACKNOWLEDGEMENT

We are indebted to Yukiko NAMBA, MD, of the Department of Maternal-Fetal and Neonatal Medicine, National Center for Child Health and Development, Tokyo, Japan, for her contribution as a neonatal expert.

WHAT'S ALREADY KNOWN ABOUT THIS TOPIC?

- Several retrospective reviews have reported the efficacy of thoracoamniotic shunting for pleural effusion in fetuses with hydrops. However, fetal death related to the shunt, including intrathoracic displacement and preterm rupture of membranes have been reported as complications. However, no systematic prospective studies have been conducted yet, and the efficacy and incidence of adverse effects (AEs) of thoracoamniotic shunting using a double-basket catheter are still unknown.

WHAT DOES THIS STUDY ADD?

- This is the first prospective trial describing the survival rate and adverse effects (AEs) associated with thoracoamniotic shunting using a thin double-basket catheter.
- Our prospective registered trial also clarified the true frequency of AEs. No fetal deaths or fatal maternal AEs were encountered; preterm rupture of the membrane before 37 weeks of gestation occurred in 7/24 (29%) cases, whereas in 1/24 (4.2%) cases, it occurred within 28 days after the shunting procedure. The reintervention rate was around 23–33%, and the indications were obstruction, dislodgement, and short-lived effect of the initial shunting procedure.

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Journal of Pediatric Surgery (2012) 47, 2327–2331

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Intrapericardial extralobar pulmonary sequestration detected as an intrathoracic cystic mass by using prenatal ultrasonography: Case report and review of the literature

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Received 2 August 2012; revised 26 September 2012; accepted 26 September 2012

Key words:
Extralobar;
Intrapericardial;
Prenatal diagnosis;
Sequestration

Abstract Intrapericardial extralobar pulmonary sequestration is a very rare congenital lung anomaly. We report a case of this condition, detected as an intrathoracic cystic lesion by using prenatal ultrasonography. The neonate was born at 38 weeks of gestation with no progression of the lesion and no respiratory or cardiac symptoms. Ultrasonography and computed tomography (CT) revealed a 40×17×17-mm intrapericardial lesion, composed of cystic components and a solid component. Intrapericardial extrapulmonary sequestration was suspected largely because CT showed a vague aberrant artery. At the age of 3 months, elective surgery was performed, and the postoperative course was uneventful.

Pulmonary sequestration is a type of congenital lung malformation. Pulmonary sequestration occurs in 2 forms: extralobar pulmonary sequestration (ELPS) and intralobar pulmonary sequestration (ILPS). Most cases of ELPS involve the left thoracic space between the lower lobe of the lung and the diaphragm. Such lesions are rarely found in other locations. Here, we report a rare case of intrapericardial ELPS.

1. Case report

Fetal ultrasonography (US) performed at 23 weeks' gestation showed an intrathoracic cystic lesion. Magnetic resonance imaging (MRI) showed a 19×29-mm cystic lesion beside the left side of the heart.

US showed no remarkable change in size of the lesion until the mother gave birth to a male neonate at 38 weeks. His birth weight was 2916 g. He had no respiratory problems. US and computed tomography (CT) performed after birth revealed that the intrathoracic lesion detected prenatally was an intrapericardial lesion, 40×17×17 mm in size, composed of a cystic component and a solid component (Fig. 1A, 1B). The intrapericardial mass extended from the left atrium to the left ventricle. On the basis of imaging findings, the differential diagnoses were intrapericardial ELPS, teratoma, and bronchogenic cyst. Intrapericardial ELPS was suspected largely because CT showed a vague aberrant artery arising from the ascending aorta (Fig. 1C).

US performed once a week during the month after birth and then once a month showed that the size of the mass was nearly unchanged. The patient exhibited no symptoms. At the age of 3 months, the infant underwent surgical excision by median sternotomy. The intrapericardial mass was found

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http://dx.doi.org/10.1016/j.jpedsurg.2012.09.056

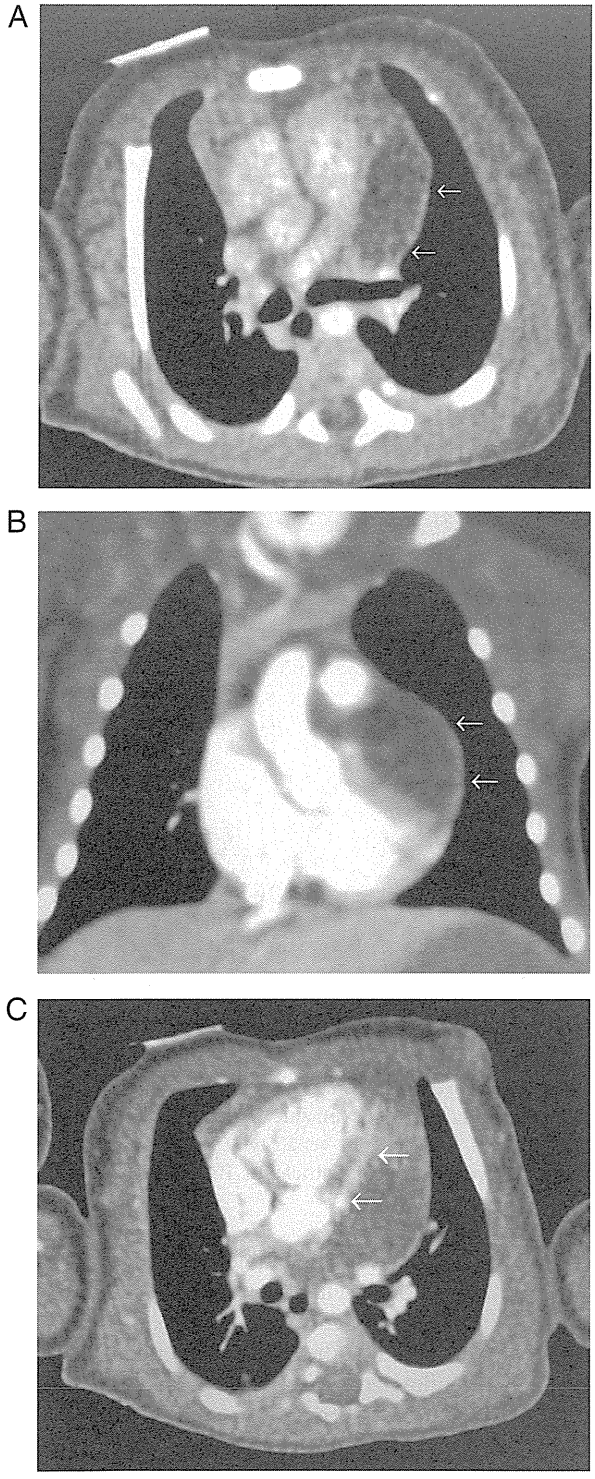

Fig. 1 (A and B) Computed tomography showed a 40×17×17-mm intrapericardial lesion, extending from the dorsal to left ventral regions of the heart. (C) An obscure artery from the ascending aorta to the mass (arrows) was assumed to be an aberrant artery preoperatively.

between the left pulmonary artery and atrium and appeared to occupy the left auricle (Fig. 2A). Careful observation showed that the mass in front of the left auricle developed from the right side of the heart to the left side, through the back of the pulmonary artery and ascending aorta. Stalks of the mass were observed on the lateral side of the right pulmonary artery. The mass was extracted from the left side to the right through the transverse pericardial sinus. After dissecting the stalks of the mass, we found 2 aberrant arteries arising from the right pulmonary artery with drainage vein reflux to the superior vena cava. The mass was resected after ligation of these vessels (Fig. 2B–D). The resected lesion weighed 10 g and was 45×30×20 mm in size (Fig. 3A). The histopathological diagnosis was intrapericardial ELPS, based on the identification of lung components such as acini, tracheal cartilage, and tracheal glands. Elastic arteries and veins were also identified using Elastica van Gieson staining (Fig. 3B). We observed numerous cavities surrounded by ciliary mucosa, filled with mucus secreted from tracheal glands, in the cystic lesion. This implied the cystic dilatation of trachea.

The postoperative course was uneventful, and the patient was discharged on the eighth postoperative day. He is now 2 years, 6 months old. There was no tumor recurrence or reoperation after the initial operation.

2. Discussion

We report a rare case of intrapericardial ELPS. Pulmonary sequestration is a congenital lung malformation, defined as a segment of lung that has no identifiable communication with the normal bronchial tree and receives its blood supply from an anomalous systemic artery [1]. The incidence of pulmonary sequestration is 0.15%–1.8%, making it the second most common congenital lung anomaly [1]. Pulmonary sequestration is divided into 2 groups based on whether the abnormal lung tissue shares a common visceral pleura with the normal lung parenchyma. ILPS refers to a mass of lung parenchyma contiguous with the normal lung and covered with the same pleura. On the other hand, ELPS involves lung tissue that is separate from normal lung tissue anatomically and covered with its own pleura. In most cases of ELPS (63%), lesions are observed between the lower lobe of the lung and the diaphragm. Approximately 10%–15% of ELPS lesions occur as intra-abdominal lesions below the diaphragm. ELPS lesions may occur anywhere within the thorax, but are rarely found in another location.

The intrapericardial space is a rare location for the detection of ELPS lesions. To our knowledge, only 7 cases have been previously reported; our case brings the total to 8. Details of all 8 cases of intrapericardial ELPS [2–8] are summarized in Table 1.

Six of the 8 cases were detected as an intrapericardial tumor; notably, 4 cases were discovered prenatally at 20–24 gestational weeks. Based on case reports of intrapericardial ELPS misdiagnosed preoperatively as intrapericardial teratoma that described the clinical findings and clinical course

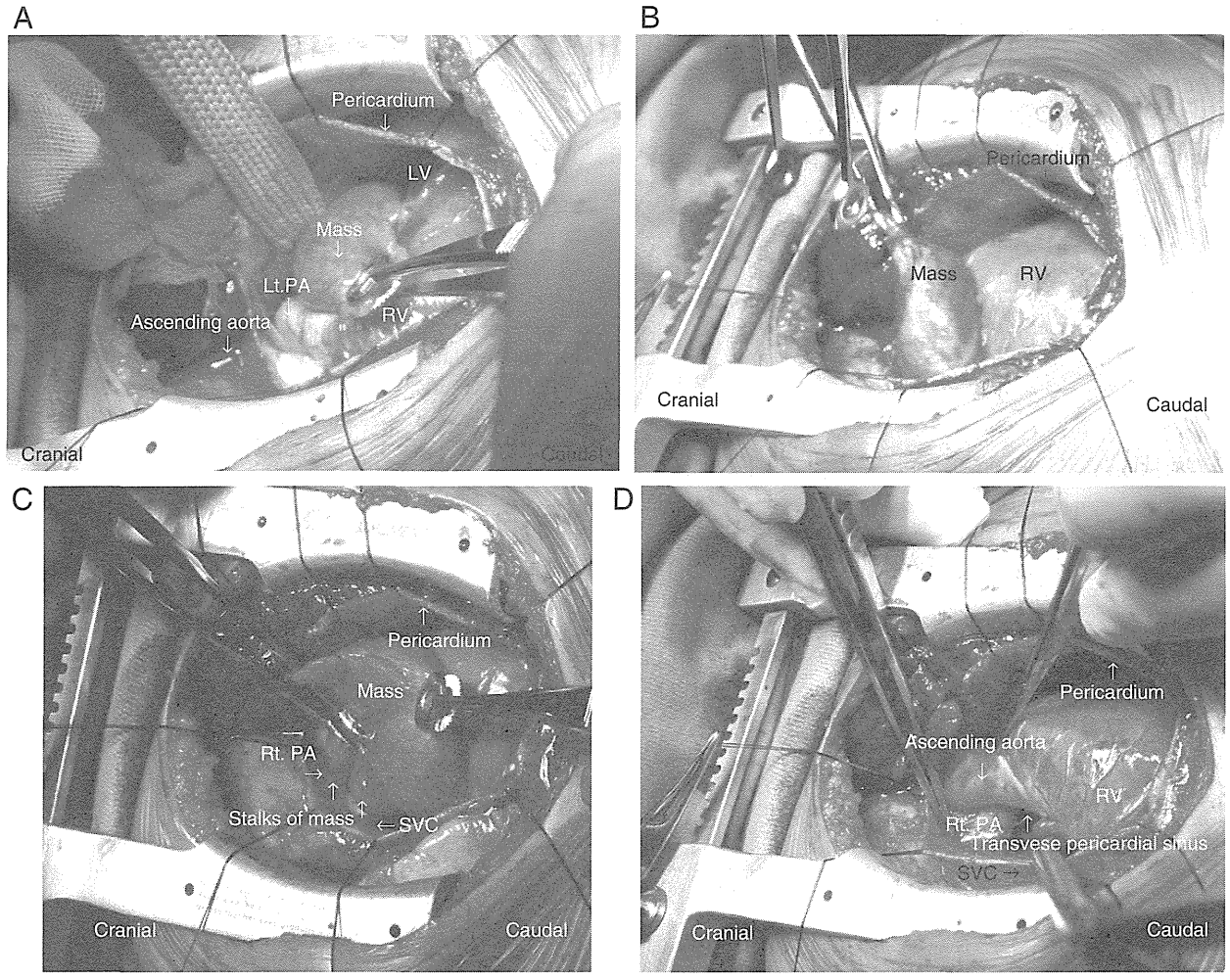

Fig. 2 (A) The intrapericardial mass grasped by forceps resembled the left auricle and was located on the left side of the heart beside the left pulmonary artery (Lt. PA). (B) The mass was extracted to the right side of the heart through the transverse pericardial sinus. (C) The mass was extracted to the right side completely and showed stalks (arrows). (D) The space after resecting the mass, with adjacent normal anatomic structures labeled. The transverse pericardial sinus where the mass developed, from the right side to the left side of the heart, is shown (arrow). Ligature of the right pulmonary artery (Rt. PA) showed the location of aberrant arteries. The superior vena cava (SVC) is not seen clearly because of retraction to the right side and location under the pericardium. RV: Right ventricle, LV: left ventricle, Lt. PA: left pulmonary artery, Rt. PA: right pulmonary artery.

in detail [5,6], 2 cases including ours reported that intrapericardial ELPS was suspected preoperatively on the basis of characteristic findings of US, CT, and MRI. In our case, CT and US were effective for diagnosis.

Symptoms (other than the mass itself) include pericardial effusion, cardiac tamponade, tachypnea, pneumothorax, tachycardia, and dyspnea. In 3 cases, there were no symptoms except for the tumor.

Aberrant arteries and a drainage vein were also important findings for diagnosis. The aberrant artery in ELPS originated from the thoracic or abdominal aorta in 80%, from the brachiocephalic, splenic, gastric, or intercostal arteries in 15%, from the pulmonary artery in 5%, and from more than one vessel in 20% of cases [1]. Venous drainage of ELPS is predominantly via systemic circulation (i.e., the azygous, hemiazygous, or inferior vena cava) in 80% of cases, completely or partially via the pulmonary vein in 25%, and rarely via the subclavian vein or portal vein [1]. The aberrant artery feeding the intrapericardial ELPS originated from various arteries, including the innominate artery, subclavian artery, and left pulmonary artery in one case each, and from the right pulmonary artery in 2 cases. In 3 cases, the aberrant artery was not detected at surgery or on autopsy. In our case, aberrant arteries originated from the right pulmonary artery, and intraoperative findings differed from preoperative CT findings.

Early resection was recommended for 2 reasons: first, to obtain a precise diagnosis and second, to prevent cardiac failure [2–8]. In intrapericardial teratoma, which is reported frequently, 48.5% of patients suffered from prenatal cardiac tamponade and fetal hydrops [9]. In the 8 reported cases of intrapericardial ELPS, 2 patients showed massive

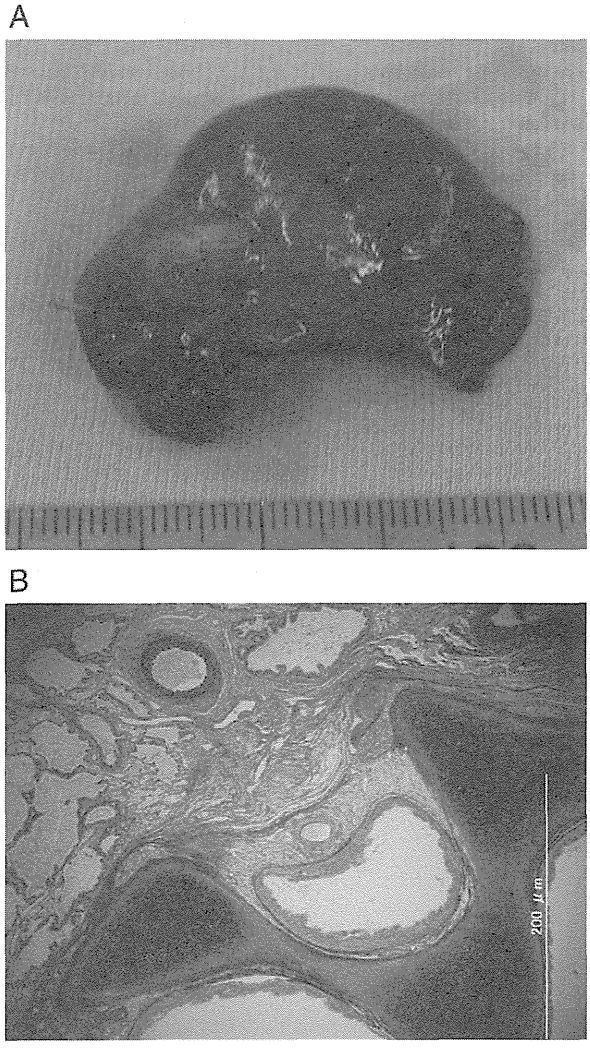

Fig. 3 (A) The resected specimen. (B) Microscopic examination (Elastica van Gieson stain) shows tracheal cartilage, tracheal glands, acini, and elastic arteries.

pericardial effusion and 1 died because of prenatal cardiac tamponade. Surgery for intrapericardial ELPS was undertaken during the neonatal period in 6 of 8 cases. In conclusion, intrapericardial ELPS, similar to intrapericardial teratoma, requires close monitoring for cardiac failure, and early resection can lead to good prognosis.

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Table 1 Summary of intrapericardial extralobar sequestration case report.

Reference	Gestational week	Birth weight	Sex	Prenatal diagnosis	Symptoms	Preoperative diagnosis	Timing of operation	Size of mass	Aberrant artery	Drainage vein
1, Levi 2)	42	4050	M	yes (42 week)	pericardial effusion tachypnea	intrapericardial mass hamartoma	2nd day	45×58×15	no connection	no connection
2, Ahn CM 3)	unknown term	unknown	M	no	right chest pain	mediastinal mass	27 years	80×80	subclavian artery	not mentioned
3, Hayashi AH 4)	(36–40)	4250	M	no	grunting, indrawing pneumothoraces tachypnea	mediastinal mass	21st day	30×30×40	no connection	no connection
4, Wax JR 5)	39	3400	F	yes (29 week)	no symptoms	intrapericardial mass teratoma or sequestration	5th day	31×24×23	left pulmonary artery	not mentioned
5, Yildiz K 6)	29 (death)	-	-	yes (29 week)	cardiac tamponade pleural effusion pericardial effusion	intrapericardial mass	none	40×30×30	not mentioned	not mentioned
6, Al-Mudaffer M 7	39	3500	M	no	pneumothoraces tachycardia	intrapericardial mass	11th day	69×57×18	innominate artery	supra vena cava
7, De Vreede I 8)	39	2770	M	yes (24 weeks)	no symptoms	intrapericardial mass CCAM or sequestration	3 weeks	20×30×20	right pulmonary artery	systemic vein
8, Our case	38	2916	M	yes (24 week)	no symptoms	intrapericardial mass CCAM or sequestration	3 months	40×30×20	right pulmonary artery	supra vena cava

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総説

嚢胞性肺疾患：特に気管支閉鎖症の診断に留意し，1歳までに手術する理由について

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要旨：嚢胞性肺疾患の治療では，どのタイプなのか診断し，その臨床像，自然歴から手術適応と時期を判断する必要がある。気管支閉鎖症の閉鎖部位は区域気管支基部が多いが，亜区域気管支以下の末梢で閉鎖し，末梢性嚢胞を示す症例を認めた。気管支閉鎖症の診断では，呼吸器科医，外科医，病理医の合同チームが必要と考えられた。肺葉切除後5年目の ^{133}Xe ガスでのRI平均通過時間（ガスが消失するまでの洗い出し時間）の評価を施行した。手術時年齢が1歳前の症例では，それ以降に手術した症例に比較して洗い出し時間が短く過膨脹傾向がないことより，残存肺は肺胞が増加することで代償されている可能性が示唆された。よって，残存肺の発育の観点から1歳までに手術することが望ましいと考えられた。

Key Words：嚢胞性肺疾患，気管支閉鎖症，肺分画症

はじめに

嚢胞性肺疾患の治療では，どのタイプなのか診断し，その臨床像，自然歴から手術適応と時期を判断する必要がある。気管支閉鎖症の診断では，呼吸器科医，外科医，病理医の合同チームが必要で，臨床像からその診断における注意点を分析した。至適手術時期に関しては議論があるが，肺葉切除後のRI肺機能の長期的変化から検討した。

気管支閉鎖症の検討

症例の特徴（図1）

本院で経験した気管支閉鎖症43例を臨床，

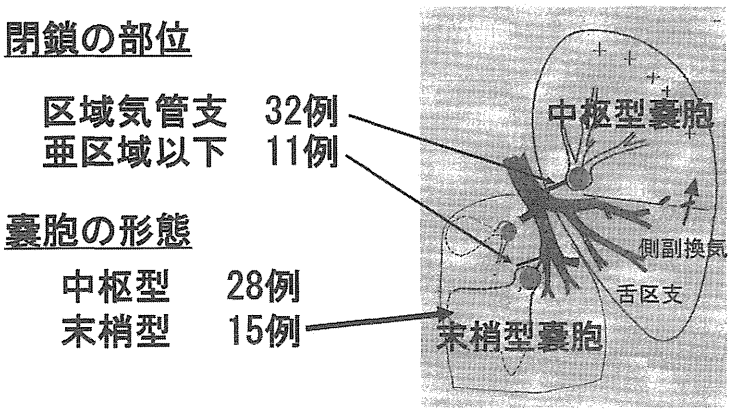

図1　気管支閉鎖症の43例の検討

病理学的に分析した。

閉鎖部位は区域気管支基部が32例と多く，内視鏡等で術前診断可能な症例を認めたが，亜区域気管支以下は11例で病理学的検討により最終診断した。

閉鎖部末梢の気管支拡張の形態は，肺門部付近での中枢性嚢胞すなわち閉鎖部直上が部分的に拡張するものは28例で，肺末梢まで拡張する末梢性嚢胞は15例35%に認めた。

閉鎖部位の肺葉別の症例数は，右肺では上葉9 (そのうち，亜区域型3)，中葉1 (0)，下葉16 (6)，左肺では上葉11(1)，下葉6(1)であった。多発部位の特徴として，左上葉11例中左上区支閉鎖が7例と多く，その閉鎖の原因として分岐位置異常が関係していた（後述)。右下葉の特徴としては亜区域以下の閉鎖を6例と多く認めた。

症例の呈示

嚢胞の形態との関係を中心に典型的な症例を示す。

1：左上区支閉鎖（図2)

図2の症例は，左上葉の舌区は認めたが，上区支が閉鎖し索状となり，その中枢側には中枢性嚢胞を認めた。

このような左上区支閉鎖7例のうち，閉鎖症部と中枢側気管支との間に索状物を認めた連続型の閉鎖の症例は4例で，他の3例は索状物を認めず離断型の閉鎖であった。上区支閉鎖部と

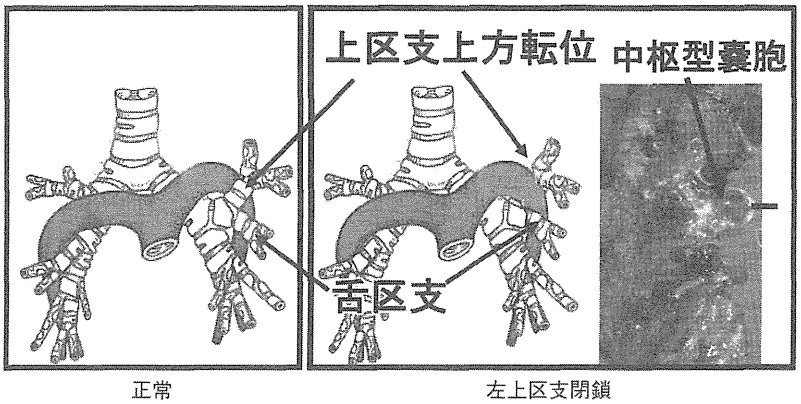

図2　左上区支閉鎖

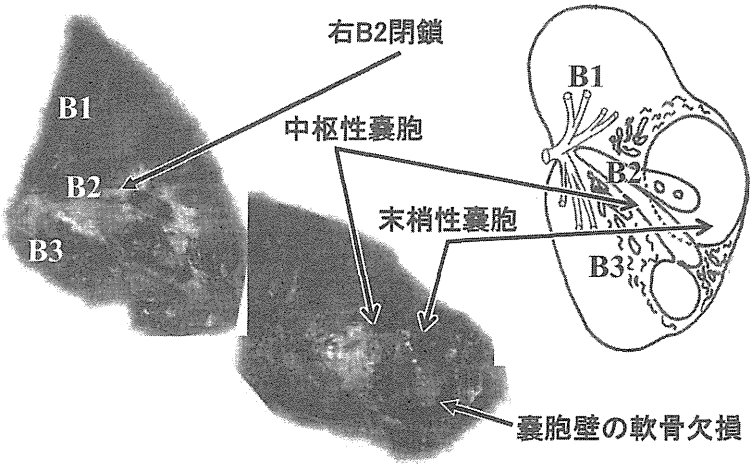

図3　混合型（中枢＋末梢性）嚢胞の症例

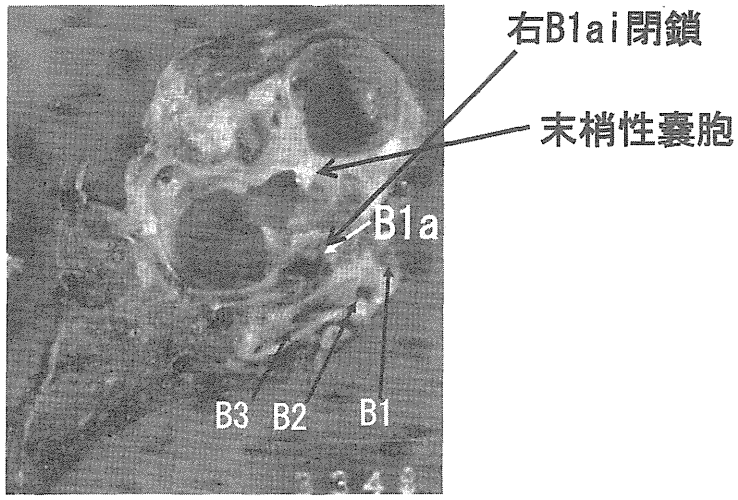

図４　亜々区域の閉鎖症例

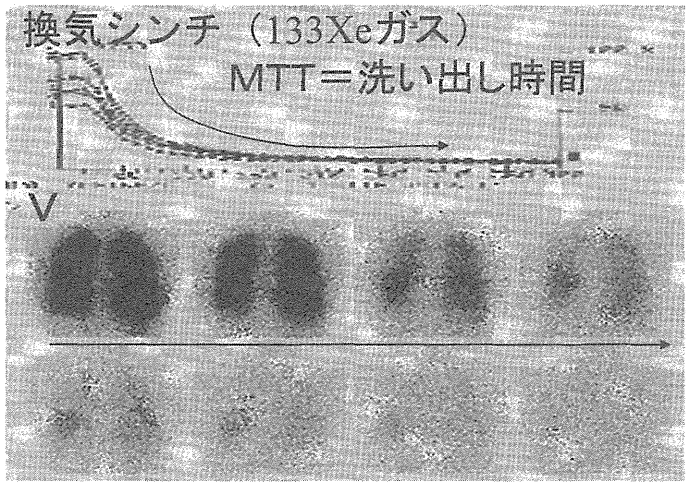

図５　換気シンチとガスが消失するまでの平均通過時間 MTT

中枢側気管支との間に索状物を認めた４例の索状物の分岐位置をみると，上区支が上方転位した分岐異常を認めた（図 2)。

正常では肺動脈が気管支の前方を横断する高さは，左上葉支の分岐部より上方であり，よって上葉支（上区支と舌区支）は肺動脈の腹側へ分岐している。上区支が上方転位した分岐異常では，上区支と舌区支が主気管支から別々に分岐し，上区支は肺動脈の背側を回り前方へ向かう走行異常を示した。上区支と舌区支で肺動脈を挟む形となり，上区支起始部は肺動脈に圧迫され索状となっていた。

2：混合型（中枢＋末梢性）嚢胞の症例（図 3)

図３に右上葉切除後のスライス標本およびそのシェーマを示す。B2 気管支は肺門近くで閉鎖しており，その末梢に円筒状に拡張した中枢性嚢胞と，肺のさらに末梢に向かい大きな嚢胞形成を示す末梢性嚢胞とが混在していた。病理的に末梢性嚢胞壁の軟骨は欠損していた。

3：亜々区域の閉鎖症例（図 4)

図４に右上葉切除後のスライス標本を示す。上葉支入口部より B1，2，3 と区域気管支が分

岐しており，B1が分岐した亜区域B1aにゾンデを入れると1 cm先で途絶しており，その先に嚢胞が存在していた。嚢胞は閉鎖部直後から大きく嚢胞状となり，多房性であった。よって，primaryな病変はB1aのさらに末梢の亜々区域での閉鎖と診断した。

肺葉切除後のRI肺機能の長期的変化

肺切除後に5年以上経時的にRI局所肺機能検査を行った95例を対象とした。

換気シンチは133Xeガスをマスクで反復吸入させ，平衡となった値を換気量Vとし，次に回路を開放しガスの洗い出しを行い，ガスが消失するまでの時間を平均通過時間MTTで評価した（図5)。

血流シンチは99mTc-MAAを静注し血流量Qを測定した。V，Qは左右肺全体を100として，MTTは患側を健側で割った数値（MTT比）で評価した。

手術時年齢での術後肺機能の相違を，1歳未満，1歳から4歳，4歳から7歳，7歳以上の4グループに分けて，V，Q，MTT比の術後1年，5年，10年での変化を検討した（図6)。

換気量Vは10年目で1歳未満が45.4 ± 2.8，1歳から4歳が40.7 ± 4.2，4歳から7歳が44.3 ± 4.6，7歳以上が29.1 ± 11.7で年齢による有意な差は認めなかった。

血流量Qは10年目で1歳未満が35.9 ± 3.9，1歳から4歳が30.8 ± 3.5，4歳から7歳が36.7 ± 2.9，7歳以上が19.7 ± 14.5で年齢による有意な差は認めなかった。

MTT比については，1歳未満でのMTT比5年が1.09 ± 0.08，MTT比10年が1.15 ± 0.11で，1歳以上でのMTT比5年が1.49 ± 0.6)，MTT比10年が1.54 ± 0.33であり，1歳以上ではガスが消失するまでの時間の延長を有意に認めた。

考　察

気管支閉鎖症について

嚢胞性肺疾患の内，特に肺葉内の気管支閉鎖

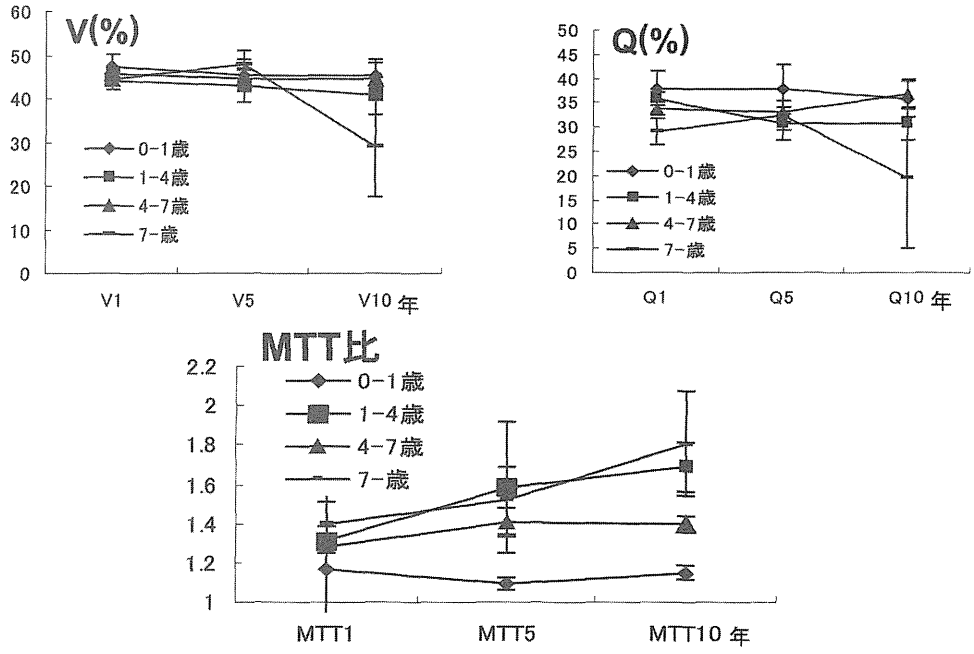

図6　手術時年齢別での術後ＲＩ肺機能

症，肺葉内肺分画症，CCAM の 3 つの鑑別が重要である[1,2]。

気管支閉鎖症は正常気管支が閉鎖した病態で，肺葉内肺分画症は，太い異常動脈があり，また正常気管支に欠損がなく，また嚢胞の形態を分析すると，異常動脈流入部付近で気管支が閉鎖した所見が得られることがある。

CCAM は基本的には病理で終末細気管支の上皮が腺腫様に増生した所見で診断されるが，CCAM に気管支閉鎖を 70％に合併する報告がある[3]。このように気管支閉鎖が注目されている。

気管支閉鎖症では 1)末梢気管支の拡張（嚢胞），2)粘液貯留と炎症（腫瘤，肺炎），3)側副換気による気腫の 3 つの要素が重なった多様な病態を示す（図 1)。末梢気管支の拡張は粘液が充満した中枢性嚢胞が典型的だが，末梢性嚢胞もわれわれの集計では 43 例中 15 例 35％に認めた。特に亜区域気管支以下で閉鎖している症例ほど末梢性嚢胞を示す傾向を認めた。文献的にも閉鎖部の末梢に大きな嚢胞を形成している症例が「気管支性嚢胞を合併した気管支閉鎖症」として報告されているが[4]，病態としては気管支閉鎖により気管支内圧が高まり，気管支脆弱部が拡張，嚢腫状となった可能性がある。

気管支性嚢胞の概念は曖昧である。肺内にある気管支上皮に覆われた嚢胞のうち，概念が明らかな疾患である肺葉内肺分画症，CCAM を除いた症例が気管支性嚢胞と診断される場合が多い。気管支閉鎖症でも末梢性に大きく拡張した嚢胞を示す場合が有り，気管支性嚢胞と診断した症例も病理的に気管支の閉鎖が確認できれば気管支閉鎖と病名変更すべきである。

従来，気管支嚢胞，肺葉内肺分画症，肺葉性気腫と診断した症例の中に気管支閉鎖症が含まれている可能性があり，気管支造影，気管支鏡などの術前検査，切除標本の詳細な検討をしていくことが，肺疾患の概念の確立のため大切と考えられる。

気管支閉鎖症は区域気管支の限局した範囲が閉鎖し，閉鎖部の末梢側気管支，肺胞の基本構造は保たれている。よって，病因として気管支の分岐が完成した後に局所的な異常によって閉鎖したと考えられている[1]。

上葉気管支の上方転位は右上葉気管支では比較的多く認め tracheal bronchus が代表的である。左上葉気管支の上方転位は頻度的には稀である[5]。肺動脈と気管支の関係を見ると（図 2)，左上葉支が上方転位すると，転位気管支は肺動脈の背側を回る走行異常を示し，肺動脈よりの圧排の程度が強くなり軟骨形成異常が進行し，狭窄さらに閉鎖状態となる可能性が考えられ，上区支の離断型閉鎖では，圧迫所見が進行した結果，気管支が離断した可能性が考えられる。

気管支閉鎖の病因として，内因的な病因も存在すると考えられる。Langston らの報告[1]では，“malformation sequence” という概念を提示している。これは胎生期 6-16 週の間において，発生学的な異常として気管支閉鎖が最初に起こることで様々な病態をきたす。すなわち胎生期のある時期・場所において気管支の閉鎖・閉塞が発生することで，結果として様々なパターンの病変（CCAM，分画症，肺葉性肺気腫）が発生し，時にオーバーラップした病態を示す可能性を提示している。Reidlinger らは[3]，切除標本の病理学的な検討の結果 ELS の 100％，ILS の 82％，CCAM の 70％ LE の 50％に気管支閉鎖が存在していると報告している。臨床的には主立った病名をつけることになると考えられるが，病理学的には気管支閉鎖，CCAM，分画症，肺葉性肺気腫が複合して存在しうることも念頭に置く必要がある。

術後 RI 肺機能からみた手術時期について

肺葉切除術の意義は，病変が正常肺を圧迫したり炎症を波及させ，正常肺の発育過程に悪影響を及ぼす場合に病変を切除し，正常肺葉の発

育を促すことが目的である。

肺切除後，残存肺が代償性に拡張するが，肺胞が増加する場合と過膨脹する場合が考えられる。術後肺機能の検討を肺換気血流 RI 検査で検討すると，手術時年齢が 1 歳以上では，5 年および 10 年で MTT 比の延長すなわち，代償性・気腫性の過膨脹による変化が表れる傾向を認めた。

肺の正常発育は，3 歳頃まで急速に肺胞の数が細胞分裂して増えていくことが知られている[6]。肺葉切除後の肺の発育も，RI 肺機能の解析の結果とあわせ，機能的発育のためには，1 歳までに手術することが望まれる。本院で経験した肺葉切除後の死亡 3 例は 6 カ月以前の症例で気管軟骨の脆弱性が影響していた。よって，軽症例では 6-12 カ月が至適手術時期と考える。

軽症の嚢胞性肺疾患の手術時期に関しては議論がある[7, 8]。感染や悪性腫瘍などの合併症を考え早期手術を推奨する報告から，手術の合併症を考え保存的な治療を推奨する報告がある。出生前診断された嚢胞性肺疾患で軽症のため経過観察されている症例の成績が今後明らかになれば，感染しやすい時期などを予想して治療方針が考慮されると考える。

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当科にて出生前診断されたisolated CDHの長期予後

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近年，わが国においては，先天性横隔膜ヘルニア（congenital diaphragmatic hernia：CDH）は，出生前診断されるようになり，母体管理を含めた周産期管理が行われるようになっている。出生前から周産期に関わる医師，看護師などの医療従事者が児の情報を共有し，分娩計画や出生後の治療方針を立案し，実施することが可能になってきた。さらにhigh frequency oscillatory ventilation（HFO），inhaled nitric oxide（iNO），extracorporeal membrane oxygenation（ECMO）などの医療機器の進歩やgentle ventilationを中心とした集学的治療方法の確立に伴い，わが国や欧米におけるCDHの生存率は上昇してきた[1, 2)]。実際に2010年に報告された日本小児外科学会学術・先進医療検討委員会の全国統計結果でも生存率85％と良好な成績が得られるようになっている[3)]。

このような予後の改善を背景として，欧米の報告を中心に先天性横隔膜ヘルニアの長期生存例に関する知見が得られるようになってきた[4~14)]。すなわち，呼吸器感染症[6~10)]，漏斗胸，側彎などの胸郭変形[4, 6~8, 11)]，胃食道逆流症（gastro-esophageal reflux disease：GERD）[6, 11)]や難聴[4~8, 12)]などの合併症の報告がなされるようになり，身体的発育や精神的発達に関してもさまざまな報告がなされるようになってきた[4~8)]。特にパッチ閉鎖やECMO施行例といった重症例に関しては，各々の合併症発生率が高いとの報告[4, 6~8)]があり，退院後の長期にわたるフォローアップの必要性が謳われている。

今回，当科で経験した先天性心疾患や染色体異常などを合併しない出生前診断されたCDH（isolated CDH）に対して，診療録と電話でのアンケート調査により当科で治療を行った患者の長期予後に関する後方視的検討を行ったので報告する。

対象と方法

1997年1月～2010年12月に当科で経験した出生前診断されたisolated CDHは45例であった。isolated CDHの定義としては，重篤な心奇形（血行動態に影響を及ぼさないVSD，ASD，PDAを除く），染色体異常，手術を行わなければ死亡する先天奇形，その他の生命予後に重大な影響を及ぼす奇形などを含まない症例とした。

図1に示すように当科における出生前診断されてCDHの治療方針として，1997～2003年はfetal stabilization（FS）＋早期手術を行い，2004～10年はgentle ventilation（GV）＋circulatory stabilization（CS）を治療の基本方針としている。**図2**に示すようにFA＋早期手術の前期群は全19例で1年以上の長期生存例は12/19（63.2％）であった。GV＋CSの後期群は全26例で，長期生存例は23/26（88.5％）であった。前期群，後期群の生存例全35例中，長期フォローアップが可能であった33例に関して再発や，胸郭変形の有無，GERD，難聴，身体的発育，精神的発達，就学状況に関する検討を診療録および電話によるアンケート調査を用いて後方視的に検討した。統計学的解析は，分割表分析を行い，カイ二乗検定により，Fisherの両側正確性検定のp値を算出した。統計学的有意差は，$p<0.05$をもって有意差ありとした。

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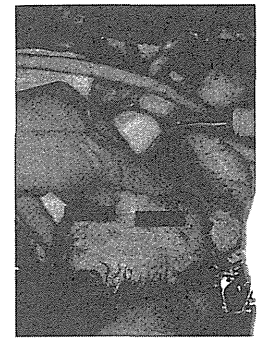
図１　当科における治療方針の変遷

☆前期群:1998年1月～2003年3月の治療方針（FS+早期手術）

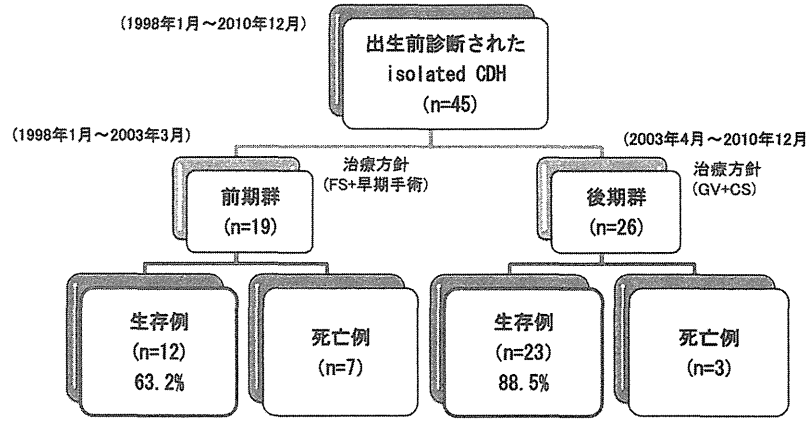
●Fetal stabilization (FS)
胎児を眠らせた状態（sleeping baby）で娩出する。
母体にmorphine投与。
胎動と呼吸様運動消失後に帝王切開で児を娩出。
臍帯離断前にpancronium投与。
mask bag換気することなく挿管、臍帯離断。
持続的筋弛緩剤の投与
●Pancronium→Vecroniumの過渡期
●積極的な呼吸性アルカローシス管理
●NO 吸入療法、HFO開始　　●ECMO使用期
●手術時期 ： 出生後可能な限り早期に手術する。



☆後期群:2003年4月から2010年12月の治療方針（GV+CS）

●Gentle ventilation (GV)
持続的な筋弛緩剤投与を行わない
フェンタネストを中心として鎮静を図る
呼吸条件はHFOまたはCMVにて、preductal SpO_2を90%、
preductal $PaCO_2$を65mmHgまで許容する
●Circulatory stabilization(CS)
血圧が安定化している（収縮期：60mmHg以上）
安定した利尿を認める(1ml/kg/hr以上)
心エコー上PDAのflowが左右もしくは、両方向性となる

図２　対象と方法



（後方視的検討）
●前期群全例(n=19)と後期群全例(n=26)を対象として

☞患者背景の比較
☞治療と成績の比較

●追跡調査が得られた前期群生存例(n=12)と後期群生存例(n=21)を対象として

☞合併症（再発、胸郭変形、胃食道逆流症、難聴）
☞長期予後（身体的発育、精神的発達・就学状況）

●統計学的検討は統計解析soft JMP により行った。$P<0.05$を有意差ありとした。

結果

表1では，前期群と後期群の患者背景と治療およびその成績の比較を示した。前期群と後期群を比較した結果，前期群で肝脱出例が84.2%と有意に高く，ECMO施行率が47.3%と高率であった一方で，生存率は68.4%と有意に低かった。また，有意差は認めないものの，前期群では胃脱出例も多く，肺胸郭比も小さい傾向にあった。したがって，前期群では後期群より重症例が含まれている可能性は否めないものの，後期群では人工呼吸日数や入院日数も短い傾向にあり，長期生存率も有意に上昇していることから予後に関しては良好な結果であった。

長期生存例の合併症に関して，再発，胸郭変形，GERD，難聴に関する検討を行った。**表2**に示すように，前期群と後期群を比較した結果では両群の再発発生率に有意差

表1　前期群と後期群の比較

(*p<0.05)

	前期群(n=19)	後期群(n=26)	全例(n=45)
診断週数(週)	30.6±4.9	28.5±5.8	29.4±5.6
肝脱出(%)	16/19 (84.2%) *	11/26 (42.3%) *	27/45 (60%)
胃脱出(%)	18/19 (94.7%)	19/26 (73.1%)	37/45 (82.2%)
羊水過多(%)	5/19 (26.3%)	11/26 (42.3%)	16/45 (35.6%)
肺胸郭比	0.09±0.04	0.12±0.03	0.11±0.05
在胎週数(週)	37.3±1.0	37.1±1.0	37.3±1.0
出生体重(g)	2802±383	2706±454	2747±424
手術有(%)	17/19 (89.5%)	25/26 (96.1%)	42/45 (93.3%)
待機時間(hr)	59.3±100.9	74.8±34.9	68.5±68.9
NO吸入(%)	14/19 (73.7%)	19/26 (73.1%)	33/45 (73.3%)
HFO(%)	14/19 (73.7%)	24/26 (92.3%)	38/45 (84.4%)
ECMO(%)	9/19 (47.3%) *	2/26(7.7%) *	11/45(24.4%)
人工呼吸日数(日)	26.2±17.3	16.2±13.2	20.5±29.1
入院日数(日)	65.1±69.7	51.4±22.4	56.5±50.4
長期生存率(%)	13/19 (68.4%)*	23/26 (88.5%) *	36/45 (80.0%)

表2　再発例の検討

再発; 36.4%(12/33)

(前期群と後期群の比較)　(*p<0.05)

前期群(n=12)	後期群(n=21)	p
4/12(33.3%)	8/21(38.1%)	0.78

(再発例と非再発例の比較)　(*p<0.05)

(項目)	再発例(n=12)	非再発例(n=21)	p
肝脱出	7/12(58.3%)	10/21(47.6%)	0.74
胃脱出	11/12(91.7%)	16/21(76.2%)	0.24
L/T比<0.1	6/12(50%)	7/21(33.3%)	0.35
Patch有	8/12(66.7%)	3/21(14.3%)	0.002*
GER有	5/12(41.7%)	4/21(19.0%)	0.16

●再発は前期群と後期群では有意差なし。
再発は、Patch有の症例では有意に発生率が上昇した。